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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appellants:	Allan Bradley et al.
Serial No:	09/839,658
Confirmation No:	9914
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For:	NOVEL COMPOSITIONS AND METHODS FOR ARRAY-BASED NUCLEIC ACID HYBRIDIZATION
Examiner:	Teresa E. Strzelecka
Art Unit:	1637

CERTIFICATE OF TRANSMISSION UNDER 37 C.F.R. §1.8(a)

The undersigned hereby certifies that this document is being electronically filed in accordance with § 1.6(a)(4), on the 5th day of May, 2008.

/Christopher Rhodes /
Christopher Rhodes

Commissioner for Patents

APPELLANTS' BRIEF PURSUANT TO 37 C.F.R. § 41.37

Dear Sir:

This Appeal Brief is filed in response to the Advisory Action mailed on February 7, 2008 and in furtherance of the Notice of Appeal filed on March 5, 2008. A fee of $500 under C.F.R. § 41.20(a)(2) is being paid electronically herewith.

The **REAL PARTY IN INTEREST** can be found on page 3 of this Appeal Brief.

A statement of **RELATED APPEALS AND INTERFERENCES** can be found on page 3 of this Appeal Brief.

The **STATUS OF CLAIMS** can be found on pages 3-4 of this Appeal Brief.

The **STATUS OF AMENDMENTS** can be found on page 4 of this Appeal Brief.

A **SUMMARY OF CLAIMED SUBJECT MATTER** can be found on pages 5 of this Appeal Brief.

A concise statement of the **GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL** can be found on pages 5-6 of this Appeal Brief.

The **ARGUMENT** can be found on pages 6-14 of this Appeal Brief.

A **CLAIMS APPENDIX** can be found on pages 15-19 of this Appeal Brief.

An **EVIDENCE APPENDIX** can be found on page 20 of this Appeal Brief.

A **RELATED PROCEEDINGS APPENDIX** can be found on page 21 of this Appeal Brief.

I. REAL PARTY IN INTEREST (37 C.F.R. § 41.37(c)(1)(i))

The real party in interest in this application is Baylor College of Medicine, assignee of the instant application. This application was licensed by Spectral Genomics, Inc. Spectral Genomics, Inc. was subsequently acquired by PerkinElmer, LAS, Inc., a Delaware corporation with corporate headquarters in Wellesley, Massachusetts.

II. RELATED APPEALS AND INTERFERENCES (37 C.F.R. § 41.37(c)(1)(ii))

While Appellants believe that there are no appeals or interferences known to Appellants, Appellants' legal representative, or the assignee of the instant application that will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal, Appellants note they have also appealed the Examiner's Final Office Action in U.S. 10/207,440, having the same inventors as the instant application.

III. STATUS OF CLAIMS (37 C.F.R. § 41.37(c)(1)(iii))

Claims 1-66 were originally filed with this case. Claims 18-66 were cancelled in response to a Restriction Requirement mailed on May 31, 2002. New claims 67-68 were added in response to an Office Action dated August 19, 2002. Claims 15-16 were canceled in response to an Office Action dated January 22, 2004. New claims 69-72 were added in response to an Office Action dated February 2, 2005. Claim 69 was canceled in response to an Office Action dated October 18, 2005. Claims 1-14, 17, 67, 68, and 70-72 are pending in this application, of which claim 1 is an independent claim. Each of these claims was rejected in a Final Office Action dated July 11, 2006. Claims 70 and 71 were canceled in an Amendment under 37 CFR § 1.116. New claims 77-94 were added in an Amendment and Response filed with a Request for Continued Examination filed on September 10, 2007. Claims 77-94 were cancelled in response to a Final Office Action mailed November 15, 2007. The amendments were entered in an Advisory Action dated February 7, 2008. The rejections of claims 1-14, 17, 67, 68, and 72 are being appealed herein.

The status of the claims is as follows:

A. Claims 1-6, 12-14, 17, 67, 68 and 72 stand erroneously rejected under § 103(a) as being unpatentable over Kallioniemi (US 2002/0132246 A1), McGill (US

5,658,730 A), Pollack (Nature Genetics, vol. 23, pp. 41-46, September 1999) as evidenced by GibcoBRL Catalog (pages 18-15 ad 18-16, 1995-96) and Mackey (Anal. Biochem., vol. 212, pp. 428-435, 1993).

B. Claims 7, 8 and 10 stand erroneously rejected under § 103(a) as being unpatentable over Kallioniemi (US 2002/0132246 A1), McGill (US 5,658,730 A), and Pollack (Nature Genetics, vol. 23, pp. 41-46, September 1999) as evidenced by GibcoBRL Catalog (pages 18-15 ad 18-16, 1995-96) and Mackey (Anal. Biochem., vol. 212, pp. 428-435, 1993), as applied to claim 1 above, and further in view of Anderson (Nucl. Acids Res., vol. 9, pp. 3015-3027, 1991);

C. Claim 9 stands erroneously rejected under § 103(a) as being unpatentable over Kallioniemi (US 2002/0132246 A1), McGill (US 5,658,730 A), Pollack (Nature Genetics, vol. 23, pp. 41-46, September 1999) as evidenced by GibcoBRL Catalog (pages 18-15 ad 18-16, 1995-96) and Mackey (Anal. Biochem., vol. 212, pp. 428-435, 1993), in view of Anderson (Nucl. Acids Res., vol. 9, pp. 3015-3027, 1991) as applied to claim 8 above, and further in view of Waggoner (US 5,268,486); and

D. Claim 11 stands erroneously rejected under § 103(a) as being unpatentable over Kallioniemi (US 2002/0132246 A1), McGill (US 5,658,730 A), Pollack (Nature Genetics, vol. 23, pp. 41-46, September 1999) as evidenced by GibcoBRL Catalog (pages 18-15 ad 18-16, 1995-96) and Mackey (Anal. Biochem., vol. 212, pp. 428-435, 1993), in view of Anderson (Nucl. Acids Res., vol. 9, pp. 3015-3027, 1991) as applied to claim 1 above, and further in view of Ordahl (Nucl. Acids Res., vol. 3, pp. 2985-2999, 1976) and Anderson (Nucl. Acids Res., vol. 9, pp. 3015-3027, 1981).

IV. STATUS OF THE AMENDMENTS (37 C.F.R. § 41.37(c)(1)(iv))

An Amendment and Response to the Final Office Action mailed November 15, 2007 was filed on January 15, 2008. These amendments were entered by the Examiner as noted in the Advisory Action mailed on February 7, 2008. A copy of the claims as pending, incorporating

any prior amendments and showing the status of each of the claims, is attached as a Claims Appendix beginning on page 15 of this Appeal Brief.

V. SUMMARY OF CLAIMED SUBJECT MATTER (37 C.F.R. § 41.37(c)(1)(v))

Aspects and examples of the claimed subject matter are generally directed to methods for hybridizing a sample of labeled nucleic acid targets to a plurality of nucleic acid probes (*See e.g.* Application at Par. Nos. [0005] and [0018]). In certain examples and as recited in claim 1, the claimed methods entail providing a nucleic acid probe comprising immobilized nucleic acid segments in an array with each probe at a known location, contacting the immobilized probes with a sample of target nucleic acid comprising fragments of genomic nucleic acid, and observing the amount and location of labeled genomic nucleic acid hybridized to each immobilized probe. As claimed, both strands are labeled with a detectable moiety, and each labeled *fragment* has a length smaller than 200 bases. (*See e.g.* Application at Par. Nos. [0005] and [0031]). In one example, each labeled fragment consists of a length between 20 bases and 150 bases. (*See e.g.* Application at Par. Nos. [0010] and [0033]). The sample of target genomic nucleic acid may be prepared using a procedure such as random priming, nick translation, and amplification to generate segments of target genomic nucleic acid; followed by a step comprising fragmentation or enzymatic digestion, or both, to generate a sample of target genomic nucleic acid consisting of sizes smaller than 200 bases. (*See e.g.* Application at Par. Nos. [0006] and [0033] and pending claims 7, 8, 10 and 11). In another example, the detectable label comprises Cy3™ or Cy5™. (*See e.g.* Application at Par. Nos. [0008] and [0035] and pending claim 9). In still another example, the sample of target genomic nucleic acid consists essentially of one chromosome. (*See e.g.* Application at Par. Nos. [0009] and [0031]). In yet another example, the sample of target genomic nucleic acid comprises a complete genome. (*See e.g.* Application at Par. Nos. [0009] and [0031]).

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL (37 C.F.R. § 41.37(c)(1)(vi))

A. Whether each of claims 1-6, 12-14, 17, 67, 68 and 72 is patentable over Kallioniemi (US 2002/0132246 A1), McGill (US 5,658,730 A), Pollack (Nature Genetics, vol.

23, pp. 41-46, September 1999) as evidenced by GibcoBRL Catalog (pages 18-15 ad 18-16, 1995-96) and Mackey (Anal. Biochem., vol. 212, pp. 428-435, 1993) where no proper *prima facie* case of obviousness has been established.

B. Whether each of claims 7, 8 and 10 is patentable over Kallioniemi (US 2002/0132246 A1), McGill (US 5,658,730 A), Pollack (Nature Genetics, vol. 23, pp. 41-46, September 1999) as evidenced by GibcoBRL Catalog (pages 18-15 ad 18-16, 1995-96) and Mackey (Anal. Biochem., vol. 212, pp. 428-435, 1993), as applied to claim 1 above, and further in view of Anderson (Nucl. Acids Res., vol. 9, pp. 3015-3027, 1991) where no proper *prima facie* case of obviousness has been established.

C. Whether claim 9 is patentable over Kallioniemi (US 2002/0132246 A1), McGill (US 5,658,730 A), Pollack (Nature Genetics, vol. 23, pp. 41-46, September 1999) as evidenced by GibcoBRL Catalog (pages 18-15 ad 18-16, 1995-96) and Mackey (Anal. Biochem., vol. 212, pp. 428-435, 1993), in view of Anderson (Nucl. Acids Res., vol. 9, pp. 3015-3027, 1991) as applied to claim 8 above, and further in view of Waggoner (US 5,268,486) where no proper *prima facie* case of obviousness has been established.

D. Whether claim 11 is patentable over Kallioniemi (US 2002/0132246 A1), McGill (US 5,658,730 A), Pollack (Nature Genetics, vol. 23, pp. 41-46, September 1999) as evidenced by GibcoBRL Catalog (pages 18-15 ad 18-16, 1995-96) and Mackey (Anal. Biochem., vol. 212, pp. 428-435, 1993), in view of Anderson (Nucl. Acids Res., vol. 9, pp. 3015-3027, 1991) as applied to claim 1 above, and further in view of Ordahl (Nucl. Acids Res., vol. 3, pp. 2985-2999, 1976) and Anderson (Nucl. Acids Res., vol. 9, pp. 3015-3027, 1981) where no proper *prima facie* case of obviousness has been established.

VII. ARGUMENT (37 C.F.R. § 41.37(c)(1)(vii))

For the reasons provided below, the Examiner's rejections are improper and should be reversed. Each of claims 1-14, 17, 67, 68, and 72, as presented, is allowable.

A. Grouping of Claims

Claims 1-14, 17, 67, 68, and 72 do not stand or fall together. To facilitate the Board's review of this appeal and only for purposes of this appeal with respect to the improper rejections under § 103, the discussion below is based on the claims having been grouped as follows:

Group I:	Claim 1-6, 12-14, 17, 67, 68 and 72, with claim 1 being representative;
Group II:	Claims 7, 8, and 10, with claim 7 being representative;
Group III:	Claim 9; and
Group IV:	Claim 11.

The patentability of each of Groups I-IV should be considered independently of the other claim groupings.

B. Claims 1-6, 12-14, 17, 67, 68 and 72 (Group I) are Each Patentable over Kallioniemi, McGill, Pollack, in view of GibcoBRL Catalog, and Mackey

Claims 1-6, 12-14, 17, 67, 68 and 72 (Group I) stand erroneously rejected under § 103(a) over Kallioniemi (US 2002/0132246 A1), McGill (US 5,658,730), Pollack (Nature Genetics, vol. 23, pp. 41-46, September 1999), in view of GibcoBRL Catalog (pages 18-15 and 18-16, 1995-96) and Mackey (Anal. Biochem., vol. 212, pp. 428-435, 1993). These rejections are improper and should be reversed because the above cited references do not render any of claims 1-6, 12-14, 17, 67, 68 and 72 (Group I) obvious.

1. The Scope of the Term "About" is Clear in view of the Specification

It is improper to interpret the term "about" to mean any number of bases. *See* page 2, lines 16-19 of the Final Office Action. It is well established that terms such as "about" are interpreted with reference to what a person of ordinary skill in the art would understand in light of the specification. *See* MPEP § 2173.05(b). The meaning and scope of such terms are intended to be flexible and can vary based on the context of their usage. In addition, under no

situation would the term "about" be interpreted to include any number of bases as erroneously proffered.

Notwithstanding the above, the numerous embodiments in the specification shed light on the flexible meaning and scope of the term "about," as that term is used in relation to the number of bases in a nucleic acid fragment. For example, Par. No. [0006], indicates the term "about" to mean a range other than "any number of bases."

> In other embodiments, the sample of target genomic nucleic acid is further prepared, e.g., fragmented, using procedures comprising mechanical fragmentation, e.g., shearing, or, enzymatic digestion, e.g., DNase enzyme, or equivalent, digestion, of a genomic nucleic acid (including the labeled nucleic acid generated by nick translation, random priming or amplification) to sizes smaller than about 200 bases, or, smaller than fragments of about 175 bases; about 150 bases; about 125 bases; about 100 bases; about 75 bases; about 50 bases; about 40 bases; about 30 bases; or about 25 bases. In another embodiment, the sample of target genomic nucleic acid (including the labeled target nucleic acid generated by nick translation, random priming or amplification) is prepared using a procedure comprising fragmentation of a genomic DNA to sizes smaller than about 200 bases by applying shearing forces sufficient to fragment genomic DNA followed by DNase or equivalent enzyme digestion of the sheared DNA to sizes smaller than about 200 bases, or, smaller than fragments of about 150 bases; about 125 bases; about 100 bases; about 75 bases; about 50 bases; about 40 bases; about 30 bases; or about 25 bases.

As described in Par. No. [0006], the number of bases of the nucleic acid fragments have a lower limit of about 25 bases and an upper limit of about 200 bases. In view of the above, it is improper to interpret "about" to mean any number of bases.

2. Claims 1-6, 12-14, 17, 67, 68 and 72 (Group I) are Patentable over Kallioniemi, McGill, Pollack, in view of GibcoBRL Catalog, and Mackey

Appellant disagrees that claims 1-6, 12-14, 17, 67, 68 and 72 (Group I) would have been obvious to one of ordinary skill in the art over the Kallioniemi, McGill, Pollack, in view of GibcoBRL Catalog and Mackey. The rejection is improper because no proper *prima facie* case of obviousness has been established.

There is no teaching, suggestion or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to

arrive at the claimed invention. See MPEP § 2143, sub-section (G). Moreover, even if proper evidence has been provided to establish a *prima facie* case of obviousness, any *prima facie* case of obviousness is rebutted because the teachings of Kallioniemi, McGill, Pollack, GibcoBRL Catalog and Mackey fail to disclose, teach or suggest the method recited in claim 1.

One skilled in the art would not have been motivated to modify Kallioniemi or to combine Kallioniemi with any of the above citations. Kallioniemi does not disclose, teach or suggest a method that uses, in part, a plurality of immobilized nucleic acid segments in an array that are a collection of clones that represent all of a chromosome or a genome of an organism, and contacting such probes with labeled fragments that include both strands of a double-stranded genomic DNA, as claimed by Appellants.

In contrast to Appellants' claims, Kallioniemi describes a genosensor that scans the human genome for large deletions or duplications *in a single assay*. (emphasis added, Kallioniemi at page 14, Par. No. [0152], [0153].) Scanning the human genome using a genosensor *in a single assay*, as disclosed in Kallioniemi, is not the same as a method that uses a plurality of immobilized nucleic acid segments *in an array* that are a collection of clones that represent all of a chromosome or a genome of an organism as defined by claim 1.

There is also no disclosure, teaching or suggestion in Kallioniemi of the "observing" step of claim 1. In particular, Kallioniemi fails to disclose, teach or suggest an amount and location of labeled genomic nucleic acid hybridized to each immobilized probe, to detect regions of amplification or deletion in the sample, wherein positional information of clones on the arrays and chromosomes is correlated, thereby generating a molecular profile of the chromosome or genome of the sample genomic nucleic acid. Instead, Kallioniemi discloses revealing "the relative concentration of each target specific sequence in the probe mixture." (Kallioniemi at page 15, Par. No. [0157].)

Moreover, as acknowledged in the Office Action, Kallioniemi does not disclose, teach or suggest nucleic acid fragments with length of less than about 200 bp to less than about 30 bp. (*See* Final Office Action dated November 15, 2007 at page 6, Par. B.) Claim 1 recites, in part, that each genomic nucleic acid fragment consists of a length smaller than 200 bases.

The above-noted deficiencies of Kallioniemi are not cured by any of the secondary citations. In addition, the Examiner has not properly articulated a finding that there was some

teaching, suggestion, or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art to modify the references. See MPEP § 2143.

McGill does not disclose, teach or suggest contacting the immobilized probes with a sample of target nucleic acid comprising fragments of genomic nucleic acid, wherein said fragments include both strands of a double-stranded genomic DNA fragment and include at least 30% repetitive sequences, and wherein each labeled fragment consists of a length smaller than 200 bases. McGill, at best, is ambiguous in describing the appropriate length for labeled fragments. McGill discloses different preferred or optimal labeled fragment lengths. For example, McGill generically states that, "it is contemplated that a nucleic acid fragment of almost any length.... For example, nucleic acid fragments may be prepared in accordance with the present invention which are up to 10,000 base pairs in length, with segments of 5,000 or 3,000 being preferred and segments of about 1,000 base pairs in length being particularly preferred." (McGill at col. 7, lines 31-40.) Thus, the teachings of McGill are contradictory as to what particular probe length is suitable. Because McGill does not specifically disclose the particular size of the labeled genomic nucleic acid fragments recited in claim 1, McGill, either alone or in combination with Kallioniemi, does not render the method of claim 1 obvious.

There also is no suggestion or motivation in McGill to combine McGill with Kallioniemi to arrive at the method of claim 1. McGill discloses diagnostic techniques for the detection of human prostate cancer. (*See* McGill Abstract.) No objective evidence has been provided that a person of ordinary skill in the art would be motivated to combine the molecular profiling method of Kallioniemi with the prostate cancer diagnostic techniques of McGill.

There also is no motivation to combine the teachings of Pollack with the teaching of Kallioniemi. Neither the Abstract nor page 46, first paragraph of Pollack discloses, teaches, or suggests the particular labeled nucleic acid fragment size recited in claim 1. Pollack does not disclose using labeled genomic nucleic acid smaller than about 200 bases. Therefore, even if Pollack is properly combinable with Kallioniemi, the combination is still deficient and does not render claim 1 obvious.

With reference to the assertion that Mackey provides the motivation to combine Kallioniemi, McGill and Pollack, this assertion is improper. It is well accepted that the

desirability of combining the cited references must exist in the cited references themselves. The mere fact that cited references can be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one of ordinary skill in the art. (*KSR International Co v. Teleflex Inc.*, 550 U.S. __, __, 82 USPQ2d 1385, 1396 (2007); *see also* MPEP § 2143.01.)

The GibcoBRL Catalog was cited by the Examiner for the sole purpose of labeling. This purpose does not cure the deficiencies noted above.

Because no suggestion or motivation exists, either in the citations themselves or in the knowledge generally available to one of ordinary skill in the art, to modify Kallioniemi or to combine Kallioniemi with the secondary citations, and because Kallioniemi, either alone or combination with the secondary citations, does not teach or suggest all the claim elements of claim 1, no *prima facie* case of obviousness has been established.

Claims 2-6, 12-14, 17, 67, 68 and 72, which depend directly or indirectly from independent claim 1, are patentable for at least the same reasons as claim 1.

In view of the above, 1-6, 12-14, 17, 67, 68 and 72 are patentable over Kallioniemi, McGill, Pollack, in view of Gibco BRL Catalog and Mackey.

C. Claims 7, 8 and 10 (Group II) are Each Patentable over Kallioniemi, McGill, Pollack, in view of GibcoBRL Catalog, and Mackey, and further in view of Anderson

Claims 7, 8 and 10 (Group II) stand erroneously rejected under § 103(a) over Kallioniemi, McGill, Pollack, in view of Gibco BRL Catalog and Mackey and further in view of Anderson (Nucl. Acids Res., vol. 9, pp. 3015-3027, 1981).

As discussed above, Kallioniemi, either alone or in combination with any secondary citation, does not render claim 1 obvious. Because claims 7, 8 and 10 each depends directly or indirectly from claim 1, Kallioniemi, either alone or in combination with any secondary citations, does not render claims 7, 8 or 10 obvious, for at least those same reasons discussed above.

Additionally, because the motivation to combine teachings of the cited references must exist in the cited references themselves, it is improper to use Anderson as the motivation to combine Kallioniemi, McGill, Pollack and Mackey. *See* MPEP § 2143.01.

In view of the above, no proper combination of cited references has been provided to render obvious the method of claim 7, which further defines the method of claim 1 by specifying that the sample of target genomic nucleic acid is prepared using a procedure such as random priming, nick translation, and amplification to generate segments of target genomic nucleic acid; followed by a step comprising fragmentation or enzymatic digestion, or both, to generate a sample of target genomic nucleic acid consisting of sizes smaller than 200 bases.

Similarly, claim 8 is not obvious in further defining the method of claim 7 by reciting that the random priming, nick translation, or amplification of target genomic nucleic acids incorporates detectably labeled base pairs into the segments.

Also, claim 10 is not obvious in that it further defines the method of claim 1 to comprise prior to step (b), the step of fragmenting the sample of target genomic nucleic acid to sizes smaller than about 200 bases by DNase enzyme digestion.

For argument's sake, even if some motivation or suggestion to combine the cited references does exist, Anderson still does not cure the deficiencies of Kallioniemi, McGill, Pollack, GibcoBRL or Mackey. Specifically, Anderson does not disclose fragmentation of target genomic DNA that has both strands labeled with a detectable moiety. Instead, the agarose gel shown in Figure 1 of Anderson was obtained by digesting lambda DNA with DNase I. No evidence has been provided that both strands of the lambda DNA have been labeled.

In view of the above, claims 7, 8 and 10 (Group II) are patentable over Kallioniemi, McGill, Pollack, in view of Gibco BRL Catalog and Mackey and further in view of Anderson.

D. Claim 9 (Group III) is Patentable over Kallioniemi, McGill, Pollack, in view of GibcoBRL Catalog, and Mackey, in view of Anderson, and further in view of Waggoner

Claim 9 (Group III) stands erroneously rejected under § 103(a) over Kallioniemi, McGill, Pollack, in view of GibcoBRL Catalog and Mackey, in view of Anderson, and further in view of Waggoner (US 5,268,486).

As discussed above, Kallioniemi, either alone or in combination with any secondary cited reference, does not render claim 1 obvious. Because claim 9 depends indirectly from claim 1,

Kallioniemi, either alone or in combination with any secondary reference, does not render claim 9 obvious, for at least the same reasons as those stated above.

Additionally, because the desirability of combining cited references must exist in the cited references themselves, it is improper to use Anderson as the motivation to combine Kallioniemi, McGill, Pollack and Mackey. *See* MPEP § 2143.01. In view of the above, no proper combination of cited references has been provided that renders claim 9 obvious.

For argument's sake, even if some suggestion or motivation to combine the cited references does exist, Waggoner still does not cure the deficiencies of Kallioniemi, McGill, Pollack, GibcoBRL or Mackey. Waggoner does not disclose labeling of both strands of genomic DNA and fragmentation or enzymatic digestion of the genomic DNA. Therefore, Waggoner's disclosure of Cy3 and Cy5 does not render claim 9 (Group III) obvious.

In view of the above, claim 9 (Group III) is patentable over Kallioniemi, McGill, Pollack, in view of Gibco BRL Catalog and Mackey, in view of Anderson, and further in view of Waggoner.

E. Claim 11 (Group IV) is Patentable over Kallioniemi, McGill, Pollack, in view of GibcoBRL Catalog, and Mackey, in view of Anderson, and further in view of Ordahl and Anderson

Claim 11 (Group IV) stands erroneously rejected under § 103(a) over Kallioniemi, McGill, Pollack, in view of GibcoBRL Catalog and Mackey, in view of Anderson, as applied to claim 1 above, and further in view of Ordahl (Nucl. Acids Res., vol, 3, pp. 2985-2999, 1976) and Anderson.

Claim 11 depends indirectly from claim 1. As discussed above, Kallioniemi, either alone or in combination with any secondary cited reference, does not render claim 1 obvious. For at least the same reasons, Kallioniemi, either alone or in combination with any secondary cited reference, does not render claim 11 obvious.

Claim 11 further defines the method of claim 1 by reciting that prior to step (b) in claim 1, the step of fragmenting the sample of target genomic nucleic acid to sizes smaller than that about 200 bases is performed by applying shearing forces sufficient to fragment genomic DNA followed by DNase enzyme digestion of the sheared DNA.

In addition to the above noted deficiencies, Ordahl is also deficient. Ordahl discloses a technique that produces DNA fragments of approximately 230 base pairs, whereas claim 11 recites fragmenting to produce sizes smaller than about 200 bases by shearing followed by enzymatic digestion of the sheared DNA with DNase. Also, as discussed above in Section C, Anderson's disclosure of digesting lambda DNA with DNAse I is not sufficient, because there is no disclosure, teaching or suggestion that both strands of the lambda DNA have been labeled. Thus, no proper evidence has been provided that the combination of the citations necessarily discloses all elements that are recited in claim 11.

In view of the above, claim 11 is patentable over Kallioniemi, McGill, Pollack, in view of GibcoBRL Catalog and Mackey, in view of Anderson, as applied to claim 1 above, and further in view of Ordahl.

F. Conclusion

For the reasons provided above, each of the rejections is improper and should be reversed. Appellants respectfully request reversal of the rejections and issuance of a Notice of Allowance.

VIII. CLAIMS APPENDIX: CLAIMS AS APPEALED (37 C.F.R. § 41.37(c)(1)(viii))

1. (Previously presented) A method for generating a molecular profile of genomic DNA by hybridization of a genomic DNA target to a plurality of immobilized nucleic acid probes, wherein the plurality is a collection of clones that represent all of a chromosome or a genome of an organism, the method comprising:

(a) providing the plurality of nucleic acid probes comprising a plurality of immobilized nucleic acid segments in an array with each probe at a known location, wherein each probe is a member of a genomic library cloned in a vector and each probe in the vector having a cloned nucleic acid insert greater than 50 kilobases, wherein the plurality of probes represents all of the chromosome or the genome;

(b) contacting the immobilized probes with a sample of target nucleic acid comprising fragments of genomic nucleic acid,

wherein said fragments include both strands of a double-stranded genomic DNA fragment and include at least 30% repetitive sequences, and

wherein both strands are labeled with a detectable moiety, wherein each labeled fragment consists of a length smaller than 200 bases, and the contacting is under conditions allowing specific hybridization of both strands of the labeled fragment of the target nucleic acid to the probe nucleic acid; and

(c) observing an amount and location of labeled genomic nucleic acid hybridized to each immobilized probe, to detect regions of amplification or deletion in the sample, wherein positional information of clones on the arrays and chromosomes is correlated,

wherein said method results in less aggregating hybridization to said probes relative to hybridization of said target genomic nucleic acid to said probes using target nucleic acids with labeled fragments of length greater than 200 bases,

or said method results in less background relative to hybridization of said target genomic nucleic acid using target nucleic acids with labeled fragments of length greater than 200 bases,

thereby generating a molecular profile of the chromosome or genome of the sample genomic nucleic acid.

2. (Previously presented) The method of claim 1, wherein each labeled fragment consists of a length no more than 150 bases.

3. (Previously presented) The method of claim 2, wherein each labeled fragment consists of a length no more than 100 bases.

4. (Previously presented) The method of claim 3, wherein each labeled fragment consists of a length no more than 50 bases.

5. (Previously presented) The method of claim 4, wherein each labeled fragment consists of a length no more than 30 bases.

6. (Previously presented) The method of claim 2, wherein each labeled fragment consists of a length between 30 bases and 150 bases.

7. (Previously presented) The method of claim 1, wherein the sample of target genomic nucleic acid is prepared using a procedure selected from the group consisting of random priming, nick translation, and amplification, of a sample of genomic nucleic acid to generate segments of target genomic nucleic acid; followed by a step comprising fragmentation or enzymatic digestion, or both, of the segments to generate a sample of target genomic nucleic acid consisting of sizes smaller than 200 bases.

8. (Previously presented) The method of claim 7, wherein the random priming, nick translation, or amplification, of the sample of genomic nucleic acid to generate segments of target genomic nucleic acid incorporates detectably labeled base pairs into the segments.

9. (Previously presented) The method of claim 8, wherein the detectable label comprises Cy3™ or Cy5 ™.

10. (Previously presented) The method of claim 1, further comprising prior to step (b), fragmenting the sample of target genomic nucleic acid to sizes smaller than about 200 bases by DNase enzyme digestion.

11. (Previously presented) The method of claim 1, further comprising prior to step (b), fragmenting the sample of target genomic nucleic acid to sizes smaller than about 200 bases by applying shearing forces sufficient to fragment genomic DNA followed by DNase enzyme digestion of the sheared DNA.

12. (Original) The method of claim 1, wherein the conditions allowing hybridization of the target nucleic acid to the probe nucleic acid comprise stringent hybridization conditions.

13. (Original) The method of claim 12, wherein the stringent hybridization conditions comprise a temperature of about 60°C to about 65°C.

14. (Original) The method of claim 1, wherein the target nucleic acid consists essentially of DNA derived from a human.

Claims 15-16 (cancelled)

17. (Previously presented) The method of claim 1, wherein the chromosome or genome is derived from a human.

Claims 18-66 (cancelled)

67. (Previously presented) The method of claim 72, wherein the sample of target genomic nucleic acid consists essentially of one chromosome.

68. (Previously presented) The method of claim 72, wherein the sample of target genomic nucleic acid comprises a complete genome.

Claims 69-71 (cancelled)

72. (Previously presented) The method of claim 1, wherein said fragments of genomic nucleic acid comprise nucleic acids from all of one or more chromosomes of said organism.

Claims 73-94 (cancelled)

IX. EVIDENCE APPENDIX (37 C.F.R. § 41.37(c)(1)(ix))

None.

X. RELATED PROCEEDINGS APPENDIX (37 C.F.R. § 41.37(c)(1)(x))

No cases believed to be directly relevant, though U.S. 10/207,440, a divisional application of the instant application, is also presently being appealed.

XI. CONCLUSION

For the reasons provided above, the rejections are improper and should be reversed. Appellants respectfully request reversal of the rejections and issuance of a Notice of Allowance. If there is any additional fee occasioned by this filing including an extension fee that is not covered by an accompanying payment, please charge any deficiency to Deposit Account No. 50/2762, Ref. No. S2037-700210.

Respectfully submitted,
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